REMARKS

The non–final Office Action dated April 10, 2007 has been reviewed, and the above-mentioned amendments and following remarks are made in response thereto. In view of the following remarks, Applicants respectfully request reconsideration of this application and timely allowance of the pending claims.

Applicants respectfully point out that the Examiner has mistakenly indicated in the Office Action that claims 1-54, 72-74, 77, 80, 83, 87, 96-103, 106, 111-127, 130, 133, 141, 143-151, 153 and 158-173 are pending. Applicants point out that claims 1-272 were pending at the time of the Office Action mailed April 10, 2007. Claims 55-71, 75, 76, 78, 79, 81, 82, 84-86, 88-95, 104, 105, 107-110, 128, 129, 131, 132, 134-140, 142, 152, 154-157 and 174-272 appear to have been withdrawn by the Examiner. Accordingly, upon entry of the instant amendment, Applicants submit that claims 1, 4-39, 41-272 are pending. Claims 1 and 4-39 and 41-72 are amended. Claims 2, 3 and 40 are cancelled without prejudice or disclaimer to the subject matter claimed therein. Written support for the claim amendments are found throughout the specification and in the original claims, thus Applicants submit that no prohibited new matter has been added.

Rejections under 35 U.S.C. 112 (second paragraph)

Claim 3 was rejected under 35 U.S.C. 112 (second paragraph) as being indefinite. Specifically, the Examiner alleged that "it is unclear as to what the amount of the antagonist is less than an effective antagonistic amount is referring to" (Office Action at page 2).

Without acquiescing to the merits of the Examiner's rejection, and solely to further the prosecution of the pending application, Applicants have cancelled claim 3 thereby rendering the rejection moot. Accordingly, Applicants respectfully request that the rejection of claim 3 under 35 U.S.C. 112 (second paragraph) be withdrawn.

Claim 40 was rejected under 35 U.S.C. 112 (second paragraph) as being indefinite. In particular, the Examiner alleged that "it is unclear what the pharmaceutically acceptable carrier in the composition is a slow release agent is referring to" (Office Action at page 2).

Without acquiescing to the merits of the Examiner's rejection, and solely to further the prosecution of the pending application, Applicants have cancelled claim 40, thereby rendering this rejection moot. Accordingly, Applicants respectfully request that the rejection of claim 40 under 35 U.S.C. 112 (second paragraph) be withdrawn.

Claim 4 was rejected under 35 U.S.C. 112 (second paragraph) as being indefinite. In particular, the Examiner alleged that the limitation "the excitatory opioid antagonist" lacks antecedent basis (Office Action at page 2).

Without acquiescing to the merits of the Examiner's rejection, and solely to further the prosecution of the pending application, Applicants have amended claim 4 to remove the terms "excitatory" and "receptor," thereby mooting the rejection. Accordingly, Applicants submit that the rejection of claim 4 under 35 U.S.C. 112 (second paragraph) be withdrawn.

Rejections under 35 U.S.C. 112 (first paragraph)

Claims 1-4, 6, 8-10, 14, 22-53, 72-74, 77, 80, 87, 96-103, 106, 111-127, 130, 133, 141, 143-151, 153 and 158-173 were rejected under 35 U.S.C. 112 (first paragraph) as not being enabled by the specification. In particular, the Examiner asserts that while the specification is enabling for certain types of neuropathic pain, such as allodynia and hyperalgesia, it does not reasonably provide enablement for the treatment of all types of neuropathic pain (Office Action at page 3). Applicants respectfully traverse the rejection.

Applicants respectfully point out that the initial burden is on the Examiner to provide a reasonable explanation as to why the scope of protection provided by the claim is not adequately enabled by the disclosure. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Moreover, the court in *In re Marzocchi* stated that it is incumbent upon the Patent Office to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). The Office Action has not provided any reasons to doubt the enablement of the claimed invention. Moreover, the Office Action has not provided a reasonable explanation or evidence establishing the nonenablement of the claims

In the absence of evidence to the contrary, the specification fully enables the claims directed to treating any type of neuropathic pain. As discussed below, Applicants have considered the claimed invention in view of the Wands factors set forth in the Office Action (numbering of the Wands factors corresponds to that in the Office Action).

(1) The nature of the invention and (2) The state of the prior art:

The Examiner states that the claims are directed to methods for treating neuropathic pain comprising administration of an opioid antagonist and admits that the state of the art regarding treating various types of neuropathic pain is relatively high. However, the Examiner contends that the state of the art for the treatment of all types of neuropathic pain with all opioid antagonists is underdeveloped.

Applicants submit that the specification provides working examples for treating neuropathic pain, including for example where alleviation of the pain is measured by hyperalgesia or allodynia with opioid antagonists alone and in combination with an agonist (specification, page 9-10 and 43-50). Given that the state of the art for treating neuropathic pain is high, the disclosure of specific examples in the specification enables the claims. Thus, in the absence of evidence to the contrary, the specification enables the claimed invention of using opioid antagonists to treat any type of neuropathic pain.

(3) The relative skill of those in the art and (5) The amount of direction or guidance presented

The Examiner alleges that the relative skill of those in the art is high with regards to treating various types of neuropathic pain. However, the Examiner asserts that there is a lack of working examples in the specification as filed showing how to treat all types of neuropathic pain.

As discussed above, the specification has provided sufficient teachings to enable one of ordinary skill in the art to practice the claimed invention. The specification teaches that opioid antagonists may be used to treat neuropathic pain, including for example where alleviation of the pain is measured by an alleviation of allodynia and hyperalgesia (specification, page 9-10).

(7) the presence or absence of working examples:

Applicants point out that MPEP 2164.02 states, "Compliance with the enablement requirement does not turn on whether an example is disclosed." Also, in *Gould*, the court stated that an applicant need not have actually reduced the invention to practice prior to filing. *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ2d 1302, 1304 Fed. Cir. 1987). Further, the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without undue experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970).

The prior art does not contradict the veracity of the Applicants statement that opioid antagonists may be used to treat neuropathic pain. Applicants respectfully point out that it is within the skill of the artisan to alleviate all symptoms neuropathic pain with opioid antagonists. The Examiner has not provided evidence that a skilled artisan would be incapable of treating neuropathic pain with an opioid antagonist as measured by other symptoms, including for example, an alleviation of hyperesthesia, spontaneous burning pain or phantom pain. As discussed above, the burden is on the Office to provide such evidence (e.g., provide scientific literature which indicates that opioid antagonists are not always successful in alleviating all types of symptoms associated with neuropathic pain. Applicants submit that the working examples provided in the application would enable a skilled artisan to alleviate any symptom associated with neuropathic pain.

and (8) The quantity of experimentation necessary:

In *In re Wands*, the Court stated, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation." *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). MPEP 2164.06 states that time and difficulty of experiments are not determinative if they are merely routine.

Applicants respectfully point out that the reference of Levine et al. (US Patent Application Publication No. 2002/0016331) cited by the Examiner in the 102 rejection examined below, confirms that opioid antagonists can be used by a skilled artisan to treat other symptoms of neuropathic pain (e.g., post-operative pain). Accordingly, Applicants submit that a skilled

artisan can conduct routine experimentation to treat other types of neuropathic pain. Such experimentation is commonplace in the pharmaceutical arena.

For the above-mentioned reasons, Applicants submit that claims 1-4, 6, 8-10, 14, 22-53, 72-74, 77, 80, 87, 96-103, 106, 111-127, 130, 133, 141, 143-151, 153 and 158-173 are enabled by the specification and respectfully request that the rejection be reconsidered and withdrawn.

Rejections under 35 U.S.C. 102(b)

Claim 1 was rejected under 35 U.S.C. 102(b) as being anticipated by Levine (US Patent Application Publication No. 2002/0016331) ("Levine"). In particular, the Examiner alleged that Levine teaches a method of treating pain, including neuropathic pain, comprising administering to a human a composition comprising an opioid antagonist (Office Action at page 5).

Anticipation is established when a single prior art reference expressly discloses, each and every element of a claimed invention. *EMI Group North America v. Cypress Semiconductor*, 268 F.3d 1342, 1350 (Fed. Cir. 2001); *Telemac Cellular Corp. v. Topp Telecom Inc.*, 247 F.3d 1316, 1327 (Fed. Cir. 2001). There must be no difference between the claimed invention and the reference disclosure as viewed by one of ordinary skill in the art. *Scripps Clinic & Research Foundation v. Genentech*, 927 F.2d 1565, 1576 (Fed. Cir. 1991).

Without acquiescing to the merits of the Examiner's rejection, and solely to further the prosecution of the pending application, Applicants have amended claim 1 to recite that the composition additionally comprises an opioid agonist and optionally a pharmaceutically acceptable carrier or excipient. Given that the composition of Levine only comprises an opioid antagonist it does not describe each and every element of the claimed invention. Accordingly, Applicants respectfully request that the rejection of claim 1 under 35 U.S.C. 102(b) be reconsidered and withdrawn.

Rejections under 35 U.S.C. 103(a)

Claims 1-4, 6, 8-10, 14, 22-45, 47-54, 72-74, 77, 80, 83, 87, 96-100, 102-103, 106, 111-127, 130, 133, 141, 143-147, 149-151, 153 and 158-173 were rejected under 35 U.S.C. 103(a) as being unpatentable over Mitch et al. (US Patent No. 5,998,434) ("Mitch") in view of Romans et al. (US Patent No. 7,015,371) ("Romans") and Sawynok et al. (US Patent No. 6,211,171)

("Sawynok") and Frome (US Patent Application Publication No. 2003/0060463) ("Frome") and Fairbanks et al. (US Patent No. 6,054,461) ("Fairbanks") and Rueter et al. (US Patent Application Publication No. 2003/0216448) ("Rueter") and Mayer et al. (US Patent No. 5,502,058) ("Mayer"). Applicants respectfully traverse the rejection.

The proper inquiry for obviousness is whether the combination of references discloses each and every feature of the claim and whether the references suggest the invention and provide one of ordinary skill in the art with a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991); *In re O'Farrell*, 853 F.2d 894 (Fed. Cir. 1988); *In re Royka*, 409 F.2d 981 (CCPA 1974); and M.P.E.P. § 2143.03.

Applicants respectfully submit that Mitch does not enable compositions comprising an opioid antagonist in an amount to enhance the pain-alleviating potency of an opioid agonist. The portion of Mitch relied upon by the Examiner merely states that the term "opioid" used throughout the application may refer to opioid agonist-antagonists. Nowhere in the application is the amount of antagonist that is effective to enhance the pain-alleviating potency of the administered agonist described. Further, The Examiner's asserts that it would have been obvious to vary and/or optimize the dose of the opioid antagonist that would enhance the potency of the opioid agonist described in Mitch. Applicants submit that it would not be obvious to use an opioid antagonist to enhance the pain alleviating affects of an opioid agonist because an antagonist in the composition would be presumed by a skilled artisan to reduce the pain alleviating affect of the agonist, not enhance it.

Moreover, the combination of Mitch with Romans, Sawynok, Frome, Fairbanks, Rueter and/or Mayer fails to provide or suggest the claimed invention. As described above, the Examiner is mistaken that it would have been obvious to modify/vary the dosages of opioid agonist and opioid antagonist of Mitch to arrive at the instant invention. As such, there is no motivation to combine Mitch with the compounds described in Romans, Sawynok, Frome, Fairbanks, Rueter and/or Mayer to arrive at the presently claimed invention. Even arguendo, if Mitch was combined with Romans, Sawynok, Frome, Fairbanks, Rueter and/or Mayer the combination would fail to provide for alleviating neuropathic pain with a composition comprising both an opioid agonist and an opioid antagonist. Accordingly, Applicants respectfully request that the rejection of claims 1-4, 6, 8-10, 14, 22-45, 47-54, 72-74, 77, 80, 83,

87, 96-100, 102-103, 106, 111-127, 130, 133, 141, 143-147, 149-151, 153 and 158-173 under 35 U.S.C. 103(a) be reconsidered and withdrawn.

Claims 43, 46, 98, 101, 145 and 148 were rejected under 35 U.S.C. 103(a) as being unpatentable over Goodman & Gillman's: The Pharmacological Approach to Therapeutics (Tenth edition, page 8) ("Goodman"). Specifically, the Examiner asserts that it would have been obvious to one having ordinary skill in the art at the time of the invention to administer the claimed composition by any known route of drug administration as taught by Goodman. Applicants respectfully traverse the rejection.

Applicants submit that there is no teaching, suggestion or motivation to treat neuropathic pain from Goodman by administering a composition comprising an opioid antagonist in an amount to enhance the pain-alleviating potency of an opioid agonist. Applicants submit that it cannot be obvious to administer a composition that is not described in the art. Thus, it would not have been obvious to try to administer an unknown composition via the routes allegedly described by Goodman. Accordingly, Applicants respectfully request that the rejection of claims 43, 46, 98, 101, 145 and 148 under 35 U.S.C. 103(a) be reconsidered and withdrawn.

The Commissioner is hereby authorized to charge deposit account 02-1818 for any fees which are due and owing.

Respectfully submitted,

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